

REMARKS

Applicant thanks the Examiner for his time and courtesy during the telephonic interview conducted on January 26, 2009. During the interview, it was agreed that the amendment to claim 83 herein and in the response of December 23, 2008, removing the limitation “amino acid residues 1-92,” did not—as asserted in the Advisory Action, mailed January 16, 2009—present new limitations not previously considered. It was agreed that the appearance that the claims added such new limitations was due to a misunderstanding due to the fact that “SEQ ID NO: 2” (which in the instant case is a nucleic acid sequence) had inadvertently previously been used in the claims to refer to the amino acid sequence encoded thereby (SEQ ID NO: 3). It was agreed that the prosecution history makes clear that both Applicant and the Examiner had been treating SEQ ID NO: 2” as its corresponding amino acid sequence (SEQ ID NO: 3), which is set forth in the sequence listing under the nucleic acid sequence of SEQ ID NO: 2. Based on the foregoing, it was agreed that the Examiner *had* previously considered the subject matter of the recitation “at least one antibody that specifically binds to SEQ ID NO: 3.” *See, e.g.* Applicant’s amendment of October 30, 2007. Also discussed in the interview were the arguments presented herein regarding the outstanding rejections of the instant claims under 35 U.S.C. § 112, paragraph 1. It was agreed that the Examiner would further consider entry of amendments and remarks in response to the outstanding final Office Action. Such amendments and remarks are presented herein. Their consideration and entry is respectfully requested.

Claims 83 and 111-115 are pending. Claim 83 is amended herein. This amendment finds basis in the specification as filed, for example in paragraph [0138] and in Figure 3 (all citations to the specification are based upon the substitute specification submitted April 4, 2007). Entry of the amendment is respectfully requested.

All pending claims are all rejected under 35 U.S.C. § 112, paragraph 1, as allegedly failing to comply with the enablement and written description requirements. There is no rejection over the prior art. With respect to all amended and cancelled claims, Applicant has not dedicated or abandoned any unclaimed subject matter and has not acquiesced to any rejections or objections

made by the Patent Office. Applicant expressly reserves the right to pursue prosecution of any presently excluded subject matter in future continuation and/or divisional applications.

Applicant has carefully considered the points raised in the Office action and believes that the Examiner's concerns have been addressed, placing this case into condition for allowance.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 83, and 111-115 are rejected for allegedly failing to comply with the enablement requirement because the specification, while being enabling for an isolated 121PIF1 transcript or transcripts that encode the protein of SEQ ID NO:2, allegedly does not reasonably provide enablement for any isolated 121PIF1 variant that encodes a protein having at least one amino acid substitution, addition or deletion relative to SEQ ID NO:2, or for the transcript variant of SEQ ID NO: 5.

Summary

As a preliminary matter, the pending claims, as amended, are not broadly drawn to all isolated variants. They are narrowly drawn to variants encoding a protein containing the sequence of SEQ ID NO: 5. As discussed in the interview, Applicant believes the assertion that nucleic acids encoding SEQ ID NO:5 is in error. As discussed in detail below, the claims are fully enabled because (1) the skilled artisan could *make* the claimed nucleic acid variants, fully commensurate with the scope of the claims, using well-known, routine methods and without undue experimentation; and (2) the skilled artisan could, armed with the teachings of the specification, *use* the claimed nucleic acid sequences, *intra alia*, for diagnosis of cancer, including, *e.g.*, for raising antibodies that detect SEQ ID NO: 3—which is overexpressed in cancers and has been deemed enabled—in patient samples, and for the detection of nucleic acids encoding SEQ ID NO: 3 in such samples. Reconsideration respectfully is requested based on the following.

Detailed remarks

As a first basis for the enablement rejection, the Examiner asserts that most claims are broadly drawn to nucleic acid sequences that include a broad genus of nucleic acids which encode "a protein of SEQ ID NO:5", which is inclusive to a variety of protein fragments and variants of SEQ ID NO:5 (126 amino acids in length), since a fragment of 100 amino acids of SEQ ID NO:5 is merely one interpretation of "a protein of SEQ ID NO:5". To clarify and to advance prosecution, claim 83 is amended without prejudice to recite "a protein containing the amino acid sequence of SEQ ID NO: 5." Given the level of knowledge in the art, the genetic code allows structure/function correlation between a polynucleotide and amino acid sequence. The skilled artisan, using existing computer technology, can easily apply genetic code to arrive at any polynucleotide encoding SEQ ID NO: 5. Accordingly, it is believed that this basis for the rejection is obviated.

The Examiner secondly alleges that the claims are nonenabled because, while the specification is enabling for SEQ ID NOs: 2 and 3, it is allegedly not enabling for making and using SEQ ID NOs: 4 and 5. Applicant respectfully disagrees.

I. Making of the claimed embodiments

Applicant notes that the breadth of the claims is such that they are drawn to individual sequences, weighing strongly in favor of enablement. Similarly, as the Examiner has agreed (see page 5 of the Office Communication dated October 24, 2008), the skilled artisan could make a protein having a sequence of SEQ ID NO:5, and could make a polynucleotide containing the sequence of SEQ ID NO:4. Given the knowledge and technology in the art, production of other polynucleotides encoding SEQ ID NO:5, based on the genetic code, is routine. Thus, the Examiner would presumably agree that one of skill in the art could also make other polynucleotides encoding a protein having the sequence of SEQ ID NO:5, based on well-known techniques. Further, routine methods in immunoassay technology would allow the skilled artisan to determine whether the claimed polynucleotides encode proteins that are immunoreactive with at least one antibody that binds a polypeptide of SEQ ID NO: 3. For example, antibodies raised against such proteins could routinely be tested for binding specificity to SEQ ID NO: 3. Thus, there appears no remaining

question as to whether the specification enables one of skill in the art to make polynucleotides, vectors and cells commensurate in scope with the claims. It clearly does.

II. Use of the claimed embodiments

The Examiner maintains, however, that such a skilled artisan would not know how to use a protein of SEQ ID NO:5, nor how to use the 12IP1F1 transcript variant of SEQ ID NO:4. Specifically, it is asserted that Applicant has not disclosed an activity or biological function of the 12IP1F1 protein of SEQ ID NO:3, or any variants thereof, and has not taught how to make and use a transcript variant that encodes a protein of SEQ ID NO:5, or encodes the protein of SEQ ID NO:5, because the instant application does not disclose the genus of transcript variants encoding SEQ ID NO:5 which share the function(s) and/or characteristic(s) of the 12IP1F1 protein of SEQ ID NO:3, e.g., highly expressed in prostate cancer. Applicant respectfully disagrees. The examples and guidance in the specification as filed would have enabled one of skill in the art to make and use the claimed polynucleotides, vectors and cells, for example, in the diagnosis of several types of cancers, without undue experimentation.

The Examiner has acknowledged and agreed with Applicant's previous arguments that the 12IP1F1 nucleic acid and protein (SEQ ID NOs: 1 and 2 of parent US Patents 7,309,585 and 6,924,358 and SEQ ID NOs: 2 and 3 of the instant application) are enabled. The Examiner states that the enablement is based on the disclosure that SEQ ID NO:3 is encoded by the nucleotide sequence of SEQ ID NO:2, which is shown to be highly expressed in prostate cancer. Applicant argues that, for the same reason, the specification enables use of the instantly claimed polynucleotides, vectors, cells and methods for, *intra alia*, diagnosis of cancers in which SEQ ID NO: 2 is overexpressed.

The fact that SEQ ID NO: 2 is overexpressed in cancer is evidenced in the specification as filed. Example 4 (paragraphs [0372]-[0377]), for example, describes RT-PCR and northern blot detection of 12IP1F1 gene overexpression in human prostate, kidney, bladder, and lung cancers (RT-PCR, see Figure 17), and in prostate cancer xenografts and a number of cancer cell lines.

Based on this expression, the specification describes and provides ample guidance for several uses of nucleic acids encoding the 121P1F1 gene (including variants such as those encoding SEQ ID NO:5). For example, the specification provides guidance for using the nucleic acids in diagnosis of prostate, bladder, kidney, colon, lung, pancreas, breast, cervix, and stomach cancer. Specification, paragraph [0027], paragraph [0373]; Table I, and Figures 20 and 21. The specification describes use of the nucleic acids for diagnosing cancer by detecting 121P1F1 nucleic acid expression in cancer patient specimens, and for raising antibodies for use in diagnosis of cancers where the 121P1F1 gene is overexpressed. See, *e.g.*, specification, paragraphs [0309]-[0310], describing that the nucleic acids can be used in cancer diagnostics, for example as probes and primers in diagnostic and prognostic methods of prostate and other cancers expressing this gene, and for generation of antibodies to proteins encoded by the polynucleotides, for use in such diagnostic and prognostic assays. Other uses are described throughout the specification. Guidance and working examples teach how to perform such uses. For example, working examples show use of nucleic acids in detection of the gene in patient cancer tissues by Northern blot and RT-PCR. A large amount of guidance is provided for generating monoclonal and polyclonal antibodies to 121P1F proteins using the nucleic acids and proteins, including those encoded by the claimed variants (see Example 9, beginning at paragraph [0419] and Example 10, beginning at paragraph [0428]), and at least one working example describes use of a polyclonal antibody (See Example 9 and Figure 13).

The foregoing provides more than enough evidence that, in addition to nucleic acids and proteins of SEQ ID NOs: 2 and 3, the nucleic acids encompassed by the instant claims also are enabled. As noted, amino acids 1-92 of SEQ ID NO:5 are *identical* to amino acids 1-92 of SEQ ID NO:3 (Figure 11), and nucleic acid residues 1-358 and 518-1028 of SEQ ID NO:4 (which encodes SEQ ID NO:5) are *identical* to nucleic acid residues 1-867 of SEQ ID NO: 2, which encodes SEQ ID NO:3 (Figure 10). Because the claimed nucleic acids contain sequences identical to residues 1-867 of SEQ ID NO:2, they can be used, for example, as described in the specification, in diagnosis of cancer types where SEQ ID NO: 2 is overexpressed. Such cancer types are identified in the specification in working examples. The diagnostic uses of the claimed nucleic acids include, for example, detection of 121P1F (*e.g.* SEQ ID NO: 2) nucleic acid (such as by PCR and Northern blotting) and generation of antibodies for detection of the 121P1F proteins (*e.g.* SEQ ID NO: 3).

The instant claims require that the nucleic acid encodes a protein that is immunoreactive with at least one antibody that specifically binds to a protein having the sequence of amino acids set forth in SEQ ID NO:3. One of skill in the art would recognize that such a protein could necessarily be used to raise antibodies against SEQ ID NO: 3 for diagnosis of cancer types overexpressing SEQ ID NO: 3 (such as those disclosed in Table I of the specification). There would also be a reasonable expectation that such an isolated nucleic acid sequence could be used in diagnosis of such cancers by detecting the polynucleotide encoding SEQ ID NO: 3 in the cancers (e.g. by Northern blot or PCR). The Examiner asserts that the specification does not provide sufficient guidance as to which isolated 121PIF1-related protein (e.g., SEQ ID NO:5) would share the same function as the 121PIF1 protein of SEQ ID NO:3, if known. Applicant maintains that because SEQ ID NO: 5 is *identical* to amino acids 1-92 of SEQ ID NO:3, there is every reason to expect that all isolated SEQ ID NO:5-containing proteins could be used to raise antibodies for diagnostic detection of SEQ ID NO:3, and would likely be immunoreactive with at least one antibody that specifically binds to a polypeptide having the amino acid sequence set forth in SEQ ID NO:3. Nonetheless, routine experimentation, e.g. immunoassays, could be used to determine whether antibodies raised against proteins encoded by the claimed nucleic acid, also would bind to the protein of SEQ ID NO: 3.

The Examiner further asserts that the specification does not provide any working examples of any 121PIF1-related protein (e.g., SEQ ID NO:5) that have the same functional activities or characteristics, i.e., highly expressed in prostate cancer as the 121PIF1 protein of SEQ ID NO:3. First, Applicant points out that based on the uses described above, such as showing is unnecessary. Whether or not the claimed nucleic acids, or the proteins they encode, are overexpressed in cancers, use of such nucleic acids and proteins is enabled because of the showing that they share identity with the fully enabled SEQ ID NO:2 and 3, which are overexpressed in cancers. This is based on the fact that the claimed nucleic acids and proteins encoded thereby can be used, for example, in diagnostics of such cancers. Nonetheless, given the identity between SEQ ID NOs: 2 and 4 noted above, detection of SEQ ID NO: 2 by RT-PCR and Northern blotting (as described in the specification) also detects SEQ ID NO: 4. Further, 121PIF proteins of various sizes were detected in cancer cell lines (See Figure 13), indicating that splice variants such as SEQ ID NO: 5 are overexpressed in the cancers.

Finally, the Examiner states that the instant application describes methods for producing 121P1F1 transcript variants encoding a protein of SEQ ID NO:5 and methods for producing the 121P1F1 variant of SEQ ID NO:5 as well as generating antibodies thereto as well as assays to determine *whether* the claimed 121P1F1 are differentially expressed in certain cancers. The Examiner goes on to analogize the teachings in the specification to those in *Genentech*, 108 F.3d at 1366, *Calgene*, 188 F.3d at 1374, and *National Recovery Technologies*, 166 F.3d at 1198, and asserts that these descriptions, without more precise guidelines, amount to little more than "a starting point, a direction for further research[.]" and that at most, the specification will enable a person of ordinary skill in the art to attempt to discover how to practice the claimed invention. Applicant respectfully disagrees.

Applicant is not merely asserting that the claimed nucleic acids (and vectors and cells containing them) have experimental or exploratory uses (such as uses to determine whether 121P1F1 nucleic acids are differentially expressed in cancer). On the contrary, the working examples in the specification show that certain cancer types are associated with 121P1F1 overexpression. Applicant is asserting that this showing provides evidence that the claimed nucleic acids, which share a high degree of identity with SEQ ID NO:2, can be employed in, among numerous other things, uses for diagnosing patients with such types of cancers. The specification provides working examples and ample guidance to enable one of skill in the art to make the claimed subject matter and to carry out these uses. Thus, contrary to the Examiner's assertions, the specification provides guidance and teaching that goes considerably beyond "a 'plan' or 'invitation' for those of skill in the art to experiment practicing[.]" The specification does much more than recognize a need or provide a starting point for further research. It provides working examples of nucleic acids encompassed by the claims, which can, by the teachings in the specification, be used in practical applications, for example, to diagnose cancer in patients. Thus, the disclosure, examples, and guidance in the specification as filed, would enable one of skill in the art to make and use the claimed invention without undue experimentation. Accordingly, withdrawal of the enablement rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 83 and 111-115 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims allegedly contained subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, it was asserted that the limitation "where the protein is immunoreactive with at least one antibody that specifically binds to amino acid residues 1-92 of SEQ ID NO:3" was not sufficiently described. Without acquiescing to this rejection, and in order to advance prosecution, claim 83 is amended to remove the recitation of "amino acid residues 1-92," obviating the recitation. All other claims depend from claim 83. Accordingly, it is believed this rejection is obviated and may be withdrawn.

CONCLUSIONS

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing **docket no. 511582003420**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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